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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/963,875	09/26/2001	Joel F. Habener	17633/1235	9674
29933	7590	12/23/2003	EXAMINER	
PALMER & DODGE, LLP KATHLEEN M. WILLIAMS 111 HUNTINGTON AVENUE BOSTON, MA 02199			BELYAVSKYI, MICHAEL A	
			ART UNIT	PAPER NUMBER
			1644	

DATE MAILED: 12/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/963,875

Examiner

Michael A. Belyav

Applicant(s)

HABENER ET AL

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 September 2003.
- 2a) ☐ This action is **FINAL**.      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-74 is/are pending in the application.
- 4a) Of the above claim(s) 1-38 and 44-73 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 39-43 and 74 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \*   c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.      6) ☐ Other: \_\_\_\_\_

#### DETAILED ACTION

1. Applicant's amendment, filed 09/22/03 is acknowledged.

*Claims 1-74 are pending.*

Applicant's election with traverse of Group VI, Claims 39-43 and 74 in response to Restriction Requirement, filed on 09/22/03 is acknowledged. Applicant traverse the Restriction Requirement on the grounds that the search of Groups VI-X together would not constitute a serious search burden on the examiner.

This is not found persuasive because the MPEP 803 (August 2001) states that "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search". The Restriction Requirement enunciated in the previous Office Action meets this criteria and therefore establishes that serious burden is placed on the examiner by the examination of more than one Group. The Inventions of Groups VI-X are different products. These inventions are differ with respect to their structures and physicochemical properties; therefore each product is patentably distinct.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-38 and 44-73 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

*Claims 39-43 and 74 drawn to an isolated, nestin-positive human pancreatic or liver stem cell that differentiates to form insulin-producing beta cell and a pharmaceutical composition comprising said cells, are under consideration in the instant application.*

2. If applicant desires priority under 35 U.S.C. 119 (e) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet.

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The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. \_\_\_\_\_" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

As the applicant has not complied with conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 (e), the effective filing date is the actual filing date of the instant application, i.e. 09/26/2001.

3. The filing date of the instant claims is deemed to be the filing date of the instant applications, i.e. 09/26/2001, as the previous priority applications 09/731,261, 60/169,082, 60/215/109 and 60/238,880 do not support the claimed limitations of the instant application, encompassing the isolated nestin-positive human pancreatic or liver stem cells wherein said cells is also GLP-1R-positive. If applicant disagrees, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the earlier priority applications. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

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4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

*(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.*

*(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.*

*(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 37(c) of this title before the invention thereof by the applicant for patent.*

5. Claims 39-43 and 74 are rejected under 35 U.S.C. 102(a) as being anticipated by Zulewski et al., (IDS).

Zulewski et al., teach an isolated nestin-positive human pancreatic stem cells that are not a neural stem cells that can differentiate to form insulin-producing cells. ( see entire document, abstract in particular). Zulewski et al., teach a composition comprising said isolated cells in PBS that is a physiologically compatible carrier. The method of isolating said cells is substantially similar to that used by applicant. While Zulewski et al., do not specifically teach that these cells are GLP-1R-positive cells, said cells would inherently be GLP-1R-positive cells, since the cell population taught by Zulewski et al., is identical to that claimed in the instant application. Since the office does not have a laboratory to test the reference isolated nestin-positive human pancreatic stem cells, it is applicant's burden to show that the reference nestin-positive human pancreatic stem cells do not have the functional limitation as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

Claim 43 is included because the claimed functional limitation would be inherent properties of an isolated cells taught by Zulewski et al., because the referenced cells are the same as claimed and would inherently be able to differentiates to insulin-producing cells. Said insulin -producing cells are the only beta cells to which nestin-positive human pancreatic stem cells can differentiate in the absence of evidence of structural difference.

The reference teaching anticipates the claimed invention.

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6. Claims 39-43 and 74 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 9715310 or by WO 00/09666 .

WO'310 teaches an isolated nestin-positive human pancreatic stem cells that are not a neural stem cells that can differentiate to form insulin-producing cells. ( see entire document, pages 8 ,10, 13 in particular). WO'310 teaches a pharmaceutical composition comprising said cells in cultured media or in PBS, that is a physiologically compatible carrier. ( see pages 13 and 14 in particular). The method of isolating said cells is substantially similar to that used by applicant ( see overlapping pages 22-24 in particular). While WO'310 does not specifically teach that these cells are GLP-1R-positive cells, said cells would inherently be GLP-1R-positive cells, since the cell population taught by WO'310 is identical to that claimed in the instant application. Since the office does not have a laboratory to test the reference isolated nestin-positive human pancreatic stem cells, it is applicant's burden to show that the reference nestin-positive human pancreatic stem cells do not have the functional limitation as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

WO '666 teaches an isolated nestin-positive human pancreatic stem cells that are not a neural stem cells that can differentiate to form insulin-producing cells. WO '666 teaches that said cells is also GLP-1R positive cells ( see entire document, Abstract and pages 13 14, 15 in particular). WO'666 teaches a pharmaceutical composition comprising said cells in cultured media or in PBS, that is a physiologically compatible carrier ( see pages 24 and 43 in particular). Since the office does not have a laboratory to test the reference isolated nestin-positive human pancreatic stem cells, it is applicant's burden to show that the reference nestin-positive human pancreatic stem cells do not have the functional limitation as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

Claim 43 is included because the claimed functional limitation would be inherent properties of an isolated cells taught by Zulewski et al., because the referenced cells are the same as claimed and would inherently be able to differentiate to insulin-producing cells. Said insulin -producing cells are the only beta cells to which nestin-positive human pancreatic stem cells can differentiate in the absence of evidence of structural difference.

The reference teaching anticipates the claimed invention.

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7. Claims 39-43 and 74 are rejected under 35 U.S.C. 102(e) as being anticipated by WO 01/39784 or by WO 02/086107

WO'784 teaches an isolated nestin-positive human pancreatic stem cells that are not a neural stem cells that can differentiate to form insulin-producing cells. ( see entire document, Abstract and pages 3 and 10 in particular). WO'784 teaches a pharmaceutical composition comprising said cells admixed with a physiologically compatible carrier ( see page 39 in particular). The method of isolating said cells is substantially similar to that used by applicant ( see overlapping pages 26-28 in particular). While WO'784 does not specifically teach that these cells are GLP-1R-positive cells, said cells would inherently be GLP-1R-positive cells, since the cell population taught by WO'784 is identical to that claimed in the instant application. Since the office does not have a laboratory to test the reference isolated nestin-positive human pancreatic stem cells, it is applicant's burden to show that the reference nestin-positive human pancreatic stem cells do not have the functional limitation as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

WO'107 teaches an isolated nestin-positive human pancreatic stem cells that are not a neural stem cells that can differentiate to form insulin-producing cells. ( see entire document, Abstract and pages 8 and 13 in particular). WO'107 teaches a pharmaceutical composition comprising said cells admixed with a physiologically compatible carrier ( see page 15 in particular). The method of isolating said cells is substantially similar to that used by applicant ( see overlapping pages 13-15 in particular). While WO'107 does not specifically teach that these cells are GLP-1R-positive cells, said cells would inherently be GLP-1R-positive cells, since the cell population taught by WO'107 is identical to that claimed in the instant application. Since the office does not have a laboratory to test the reference isolated nestin-positive human pancreatic stem cells, it is applicant's burden to show that the reference nestin-positive human pancreatic stem cells do not have the functional limitation as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

Claim 43 is included because the claimed functional limitation would be inherent properties of an isolated cells taught by Zulewski et al., because the referenced cells are the same as claimed and would inherently be able to differentiate to insulin-producing cells. Said insulin-producing cells are the only beta cells to which nestin-positive human pancreatic stem cells can differentiate in the absence of evidence of structural difference.

The references teaching anticipates the claimed invention.

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8. No claim is allowed.

9 The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. For example , on pages 2 and 3 the letter “ $\beta$ ” is missing in the word “ - cell”; on page 56, line 8, the phrase “ the nestin-positive cells are distinct from ... ” is incomplete. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskiy whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306

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December 15, 2003

  
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